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ACCESSION NUMBER: 2001032207 PCTFULL ED 20020820
TITLE (ENGLISH): METHODS FOR CONFERRING ACTIVE/PASSIVE IMMUNOTHERAPY
TITLE (FRENCH): PROCEDE PERMETTANT D'APPLIQUER UNE IMMUNOTHERAPIE ACTIVE/PASSIVE
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PATENT ASSIGNEE(S): UNITED STATES ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001032207	A1	20010510

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US1112 A 20000119
PRIORITY INFO.: US 1999-09/429,491 19991029

DETD The concept of **ligand-hapten conjugations** for redirecting hunioral immunity to lyse target cells has been previously tested in vitro (Circolo & Borsos, Lysis of hapten-labeled cells by. . . I3, 1861-2, 199 1). Lussow et al., (SangStat Medical Corp. Menlo Park CA) have recently shown that redirecting circulating antibodies via **ligand-hapten conjugates** eliminates target cells in vivo (Lussow AR, Buelow R, Fanget L, Peretto S, Gao L, Pouletty P. Redirecting Circulating Antibodies via **Ligand-hapten Conjugates** Eliminates Target Cells In vilvo, J Inimunother Emphasis Tumor Immunol, 19, 257-65, 1996).

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to the hapten including the proliferation of antibodies to the hapten, and B) administering to the patient a sufficient amount of a **hapten-ligand conjugate** wherein the ligand of the conjugate has at least one binding site to the target antigen and the hapten of the conjugate is available for binding with the antibodies such that the target antigen becomes **complexed** with the **hapten-ligand conjugate** and with the antibodies to the extent that the target antigen undergoes neutralization by the immune cells of the patient.

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activated immune cells having binding sites for the immunogen, and then, B) administering to the patient a sufficient amount of a **hapten-ligand**

conjugate wherein the ligand of the conjugate has at least one binding site to the target
antigen and the hapten or immunogen. . .

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antigen binding ligand conjugated to DNP would gain (humoral) antibody-mediated immunity. On the other hand, a subject administered a ligand-ABA-Tyr **conjugate** I I
both **ligand-hapten** and **ligand**-immunogen
achieves both humoral and cellular immunity to
the target antigen.

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ligand. The anti-ricin ABA are then conjugated to the chemical
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hapten DNP (dinitrophenol). Rabbit anti-DNP antisera is commercially available. Standard
U(complement) and **ADCC** (antibody dependent cellular
cytoxicity) assays and the passive
cutaneous Arthus reaction are used as prototypic models for testing humoral chemical ligand-
API.

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the presence of mouse
sera, heat inactivated mouse sera (56' C, 3)O min) or spleenic leukocytes to assay for
complement and **ADCC** mediated lysis of SRBC (hemoglobin
release). The optimum M [C]
(molar concentration) of intact anti-ricin (Fc+) for lysis of
Ricin-SRBC
in the C' and **ADCC**
assays serves as a guide for selection of M [C] of anti-ricin (Fab). If complement and **ADCC**
mediated lysis of SRBC is by API. the lysis will be apparent in the (4) test sample and (5)
positive control, and. . .

CLMEN. . . to said
hapten including the proliferation of antibodies to the hapten; and
B) administering to the patient a sufficient amount of a **hapten -ligand**
conjugate
wherein said ligand of said conjugate has at least one binding site to said target antigen and
id hapten of said conjugate. . .

. . .

of activated immune cells having binding sites for said
immunogen. and then,
B) administering to said patient a sufficient amount of a **hapten -ligand**
conjugate
wherein said ligand of said conjugate has at least one binding site to said target antigen and
said hapten or immunogen of. . .

20 The method of claim 7, wherein said **hapten** of said **hapten-ligand conjugate** is
dintrophenyl. and said immunogen is L-tyrosine-p-azobenzenearsonate and wherein said
hapten is bound to said immunogen by a spacer molecule of from. . .